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| EXAMINER |
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SITTON, JEHANNE SOUAYA

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1634

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10/26/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |
|------------------------------|------------------------|---------------------|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |
|                              | 10/052,417             | GELFAND ET AL.      |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |
|                              | Jehanne S. Sitton      | 1634                |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 06 July 2007.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-3,6-8,11-13,16-18,21-23,26,27,31-36,39-42,45-47, 50-52, 55-81 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____.                                     |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____.   | 6) <input type="checkbox"/> Other: _____.                         |

**Continuation of Disposition of Claims:** Claims pending in the application are 1-3,6-8,11-13,16-18,21-23,26,27,31-36,39-42,45-47,50-52 and 55-81.

**DETAILED ACTION**

1. Currently, claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31-36, 39-42, 45-47, 50-52 and newly added claims 55-81 are pending in the instant application. The amendments and arguments have been thoroughly reviewed but are insufficient to place the instant application in condition for allowance. The following rejections are either reiterated or newly applied as necessitated by amendment. This action is FINAL.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The rejections made under 35 USC 102 and 103 made in the previous office action are withdrawn in view of the newly applied rejections set forth below, as necessitated by amendments.
4. Applicant's arguments regarding the rejection under 35 USC 101 are persuasive. Accordingly, the rejection has been withdrawn.

***New Grounds of Rejection necessitated by amendment***

***Claim Rejections - 35 USC § 112***

5. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31-36, 39-42, 45-47, 50-52 and newly added claims 57, 60, 63, 66, 69, 72, 75, 78, and 81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

The claims have been amended to add a large number of polymerases in the alternative, including *Thermotoga maritima*, *Thermotoga neapolitana*, *Thermosiphon africanus*, *Bacillus caldotenax*, *Bacillus stearothermophilus*, as well as *Thermus oshimai*, *Thermus silvanus*, *Thermus chliarophilus*, *Thermus scotoductus*, *Thermus ruber* and *Thermus brockianus*, where each polymerase is specifically set forth to contain a number of specific amino acids at positions along SEQ ID NO: 1. The specification cites table 1 at page 15 as well as page 17 for support for the amendment. However, throughout the specification, the specification only teaches mutating position 4 of SEQ ID NOS 1, 2, and 3. For example, at pages 3 and 4, the specification teaches that a thermostable DNA polymerases is mutated, from it's native form, at position of the 4 of the critical motif. However, as can be seen from table 1, the native form of *Thermotoga maritima*, *Thermotoga neapolitana*, *Thermosiphon africanus*, *Bacillus caldotenax*, and *Bacillus stearothermophilus* do not possess the amino acid composition set forth in the independent or dependent claims. For example, the independent claims require that position 6 is Ala or Ser, however the native form of *Thermotoga maritima*, *Thermotoga neapolitana*, *Thermosiphon africanus*, *Bacillus caldotenax*, and *Bacillus stearothermophilus* do not possess an Ala or Ser at position 6 of the critical motif. While the specification provides description of arriving at polymerases of the invention by mutating position 4 of the critical motif, the specification does not provide support for a recombinant *Thermotoga maritime* polymerase, for example, with a Ser or Ala at position 6. It is noted that the specification does not provide the sequence of the critical motif for *Thermus oshimai*, *Thermus silvanus*, *Thermus chliarophilus*, *Thermus*

*scotoductus*, *Thermus ruber* and *Thermus brockianus*, and none of the cited references at page 17 of the specification teach the sequence of the polymerase. Accordingly, the specification does not appear to provide support for the specific sequences of the critical motif within these polymerases as well.

***Claim Rejections - 35 USC § 103***

6. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31, 33-36, 39-42, 45-47, 55-56, 58-59, 61-62, 64-65, 70-71, 73-74, and 76-77, are rejected under 35 USC 103(a) as being unpatentable over Brandis I (Brandis et al; US Patent 6,265,193) in view of Abramson (Abramson et al; US Patent 5,466,591).

Brandis I teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-13, col. 6, lines 4-39, col. 8, Tables 1 and 2 at cols 17-22).

With regard to claims 1-3, 6-8, 33-36, 39-42, and 45-47, Brandis I teaches making the specific mutants in *Taq* polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15, Brandis I teaches making a number of mutants at position 681 of *Taq*, which have at least 3 fold lower discrimination (table 2, cols 21-22). Brandis teaches making the specific E681K mutant. Brandis I teaches kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye (claims 6-9), fluorescein type dyes (col. 4), and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3'

dideoxynucleotides (chain terminator) (col. 4, lines 35-39). Brandis I teaches that sequence homology between DNA polymerases permits corresponding positions to be assigned to amino acid residues for DNA polymerases other than Taq. With regard to the newly added claim limitation “wherein said polymerase is selected from the group consisting of *Thermus thermophilus*...”, Brandis I does not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species (col. 8, lines 53-54). Brandis I teaches “the specific amino acid residues that form the nucleotide interaction region will vary in accordance with the particular DNA polymerase selected as a parent enzyme for the introduction of discrimination reducing mutations. The determination of analogous amino acid residues positions between different DNA polymerases may easily be achieved by the person skilled in the art because of the large number of DNA polymerase amino acid sequences that have been determined and the many regions of homology have been found between these different DNA polymerases. For example, a large compilation of the amino acid sequences of DNA polymerases from a wide range of organisms and homology alignments between the sequences can be found... Examples of amino acid residues within the nucleotide label interaction regions of phage T7 polymerase and E. coli DNA polymerase are provided in Table 1. In addition to providing mutant DNA polymerases having reduced discrimination for fluorescein type dyes in *Taq*, T7 and E. coli DNA polymerase I, the invention provides mutant DNA polymerases from many other organisms. In general, the teachings of the invention may be used to produce mutant DNA polymerases having reduced discrimination for fluorescein type dyes from any DNA polymerase that shares sufficient amino acid sequence

homology to Taq DNA polymerase to permit a person of ordinary skill in the art to identify one or more amino acid residue positions in the DNA polymerase that are analogous to position[s] 681..."

With regard to claims 11-13 and 16-18, Brandis I teaches providing polynucleotides encoding the mutant polymerases (abstract, all of col. 11, especially lines 40-45).

With regard to claims 21-23, 26-27, and 31 Brandis I teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

With regard to the various independent and dependent claims which recite "*Thermus thermophilus* and *Thermus specie Z05*" Abramson teaches the sequence of the *Thermus thermophilus* and *Thermus specie Z05* polymerase, including the critical motif set forth in the claims (see SEQ ID NO: 10 and 8 respectively). Further, Abramson teaches making mutations in conserved regions of thermostable polymerases.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide a recombinant mutant polymerase from *Thermus thermophilus* and *Thermus specie Z05* wherein such mutation results in a polymerase with reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase, as taught by Brandis I, in view of the teaching of the amino acid sequence for *Thermus thermophilus* and *Thermus specie Z05* as taught by Abramson. It would have further been *prima facie* obvious to the ordinary artisan at the time the invention was made to use such mutant polymerase in the methods taught by Brandis I. The ordinary artisan would have been motivated to make the specific mutations

taught by Brandis I in the mutant polymerases taught by Abramson for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis I. Brandis I provides specific teaching and motivation to make such mutations in thermostable polymerases, and Abramson provides the sequences of a number of thermostable polymerases. Given the teachings of Abramson and Brandis I, applying the technique taught by Brandis I to arrive at mutant nucleic acids, polymerases, kits, and methods of use as taught by Brandis I, to the "comparable" polymerases taught by Abramson would have been obvious to the ordinary artisan and further, the results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

7. Claims 1-3, 6-8, 11-13, 16-18, 21-23, 26-27, 31, 33-36, 39-42, 45-47, 55-56, 58-59, 61-62, 64-65, 70-71, 73-74, and 76-77, are rejected under 35 USC 103(a) as being unpatentable over Brandis II (Brandis et al; US PreGrant Publication 2002/0164591) or Brandis III (Brandis et al; US PreGrant Publication 2006/0088879), each in view of Abramson.

Brandis II and III each teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-8, 15, Tables 1 and 2).

With regard to claims 1-3, 6-8, 33-36, 39-42, and 45-47, Brandis II and III each teaches making the specific mutants in Taq polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15. Brandis II and III each teaches making a number of mutants at position 681 of Taq, which have at least 3 fold lower discrimination (table 2.). Brandis teaches making the specific E681K mutant. Brandis II and III each teaches kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye, fluorescein type dyes, and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator). Brandis II and III teach that sequence homology between DNA polymerases permits corresponding positions to be assigned to amino acid residues for DNA polymerases other than Taq. With regard to the newly added claim limitation "wherein said polymerase is selected from the group consisting of *Thermus thermophilus*...", Brandis II and III do not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species (para 0037 of Brandis II and III). Brandis II and III teach "the specific amino acid residues that form the nucleotide interaction region will vary in accordance with the particular DNA polymerase selected as a parent enzyme for the introduction of discrimination reducing mutations. The determination of analogous amino acid residues positions between different DNA polymerases may easily be achieved by the person skilled in the art because of the large number of DNA polymerase amino acid sequences that have been determined and the many regions of homology have been found between these different DNA polymerases. For example, a large compilation of the amino acid sequences of DNA polymerases from a wide range of organisms and homology alignments between the sequences can be found... Examples of amino acid residues within the

nucleotide label interaction regions of phage T7 polymerase and E. coli DNA polymerase are provided in Table 1. In addition to providing mutant DNA polymerases having reduced discrimination for fluorescein type dyes in Taq, T7 and E. coli DNA polymerase I, the invention provides mutant DNA polymerases from many other organisms. In general, the teachings of the invention may be used to produce mutant DNA polymerases having reduced discrimination for fluorescein type dyes from any DNA polymerase that shares sufficient amino acid sequence homology to Taq DNA polymerase to permit a person of ordinary skill in the art to identify one or more amino acid residue positions in the DNA polymerase that are analogous to position[s] 681..."

With regard to claims 11-13 and 16-18, Brandis II and III each teaches providing polynucleotides encoding the mutant polymerases (abstract, claim 9 of Brandis II)

With regard to claims 21-23, 26-27, and 31 Brandis II teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

With regard to the various independent and dependent claims which recite "*Thermus thermophilus* and *Thermus specie Z05*" Abramson teaches the sequence of the *Thermus thermophilus* and *Thermus specie Z05* polymerase, including the critical motif set forth in the claims (see SEQ ID NO: 10 and 8 respectively). Further, Abramson teaches making mutations in conserved regions of thermostable polymerases.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide a recombinant mutant polymerase from *Thermus thermophilus* and *Thermus specie Z05* wherein such mutation results in a polymerase with

reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase, as taught by Brandis II or III, in view of the teaching of the amino acid sequence for *Thermus thermophilus* and *Thermus specie Z05* as taught by Abramson. It would have further been *prima facie* obvious to the ordinary artisan at the time the invention was made to use such mutant polymerase in the methods taught by Brandis II or III. The ordinary artisan would have been motivated to make the specific mutations taught by each of Brandis II and III in the mutant polymerases taught by Abramson for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis II or III. Brandis II and III each provide specific teaching and motivation to make such mutations in thermostable polymerases, and Abramson provides the sequences of a number of thermostable polymerases. Given the teachings of Abramson and Brandis II and III, applying the technique taught by Brandis II or III to arrive at mutant nucleic acids, polymerases, kits, and methods of use as taught by Brandis II or III, to the "comparable" polymerases taught by Abramson would have been obvious to the ordinary artisan and further, the results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

8. Claims 32, 50-52, 67-68, and 79-80 are rejected under 35 USC 103(a) as being unpatentable over Brandis I, II, or III each in view of Abramson and Gelfand (US Patent 5,939,292).

Brandis I, II, and III teach mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase. Brandis I, II, and III teach making the specific E681K mutant. Brandis I, II, and III teach kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye, fluorescein type dyes, and nucleotides which are any naturally occurring nucleotides (encompasses dNTP and rNTP). With regard to the newly added claim limitation “wherein said polymerase is selected from the group consisting of *Thermus thermophilus*...”, Brandis I, II and III do not limit the mutant polymerases described to only *Taq*, but also specifically teaches that the mutant polymerases include polymerases from other *Thermus* species (col 8 of Brandis I, para 0037 of Brandis II and III). Brandis I, II and III teach “the specific amino acid residues that form the nucleotide interaction region will vary in accordance with the particular DNA polymerase selected as a parent enzyme for the introduction of discrimination reducing mutations. The determination of analogous amino acid residues positions between different DNA polymerases may easily be achieved by the person skilled in the art because of the large number of DNA polymerase amino acid sequences that have been determined and the many regions of homology have been found between these different DNA polymerases. For example, a large compilation of the amino acid sequences of DNA polymerases from a wide range of organisms and homology alignments between the sequences can be found... Examples of amino acid residues within the nucleotide label interaction regions of phage T7 polymerase and E. coli DNA polymerase are provided in Table 1. In addition to providing mutant DNA polymerases having reduced discrimination for fluorescein type dyes in

Taq, T7 and E. coli DNA polymerase I, the invention provides mutant DNA polymerases from many other organisms. In general, the teachings of the invention may be used to produce mutant DNA polymerases having reduced discrimination for fluorescein type dyes from any DNA polymerase that shares sufficient amino acid sequence homology to Taq DNA polymerase to permit a person of ordinary skill in the art to identify one or more amino acid residue positions in the DNA polymerase that are analogous to position[s] 681...”

With regard to claims 32 and 50-52, Brandis I, II and III teach to provide mutant polymerases comprising other mutations in addition to the discrimination mutations such as those at position 681 of Taq polymerase, including mutants outside the discrimination regions (col. 10, lines 9-23, Table 2, cols 19-22). Brandis I, II and III teach mutations at position 615 of Taq polymerase (instant SEQ ID NOS 18). Brandis I, II or III do not specifically teach a polymerase comprising *both* a mutation at position 681 and a mutation at position 615, however Gelfand teaches to use modified DNA polymerases with enhanced efficiency for incorporating unconventional nucleotides, such as ribonucleotides, using a polymerase with a mutation at position 615, corresponding to Taq polymerase, in methods of DNA sequencing (see abstract, cols 2-3). Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide a mutant DNA polymerase with both a mutation at position 681 and 615, relative to Taq, both taught by Brandis, in the mutant polymerases of Brandis I, II or III for use in the sequencing methods or primer extension (minisequencing) methods taught by Brandis I, II or III because Gelfand teaches that the mutation at position 615 in a DNA polymerase provides for DNA polymerases that enable alternative nucleic acid synthesis methods for accurate and cost effective nucleic acid DNA sequence analysis. It would

have further been *prima facie* obvious to the ordinary artisan at the time the invention was made to provide such mutant polymerases and a ribonucleotide labeled with a fluorescein type family dye for the purposes of making the methods of Brandis I, II or III, each in view of Gelfand more convenient to perform.

With regard to the various independent and dependent claims which recite "*Thermus thermophilus* and *Thermus specie Z05*" Abramson teaches the sequence of the *Thermus thermophilus* and *Thermus specie Z05* polymerase, including the critical motif set forth in the claims (see SEQ ID NO: 10 and 8 respectively). Further, Abramson teaches making mutations in conserved regions of thermostable polymerases.

Therefore, it would have further been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide a recombinant mutant polymerase from *Thermus thermophilus* and *Thermus specie Z05* wherein such mutation results in a polymerase with reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase, as taught by Brandis I, II or III, in view of Gelfand further in view of the teaching of the amino acid sequence for *Thermus thermophilus* and *Thermus specie Z05* as taught by Abramson. It would have further been *prima facie* obvious to the ordinary artisan at the time the invention was made to use such mutant polymerase in the methods taught by Brandis I, II or III in view of Gelfand. The ordinary artisan would have been motivated to make the specific mutations taught by each of Brandis I, II and III in view of Gelfand, in the mutant polymerases taught by Abramson for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis I, II or III. Brandis I, II and III each

provide specific teaching and motivation to make such mutations in thermostable polymerases, and Abramson provides the sequences of a number of thermostable polymerases. Given the teachings of Abramson and Brandis I, II and III, applying the technique taught by Brandis I, II or III in view of Gelfand to arrive at mutant nucleic acids, polymerases, kits, and methods of use as taught by Brandis I, II or III in view of Gelfand, to the “comparable” polymerases taught by Abramson would have been obvious to the ordinary artisan and further, the results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

### ***Double Patenting***

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 31, 64, and 65 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16, 20-24, 27-32, 36-44 and 48-52 of copending Application No. 09/823,649,(now US Patent 7,179,590) and Giardano (US Patent 6,107,029).

Claim 31 is drawn to a method of producing labeled DNA by providing a mutant thermostable DNA polymerase comprising LSX[-E]L[AS]IPXXE, a fluorescein family dye labeled nucleotide and performing a DNA synthesis reaction. The instant specification defines a “DNA synthesis reaction” to encompass PCR, SDA, transcription mediated amplification, primer extension, and reverse transcription.

The claims of the ‘649 application are directed to methods of reverse transcription using a mutant thermostable polymerase which comprises L[SA]X[-EAGPD][LI][SA]XXXXE and treating a reaction mixture to initiate synthesis of an extension product to provide a cDNA. The claims further limit the polymerase to a mutant thermostable polymerase such as *Thermus thermophilus*, which has an I at position 7 and a P at position 8 of instantly claimed SEQ ID NO: 1, as well as defining claimed polymerases in terms of additional polymerases such as *Thermus specie Z05* (see table 1). Accordingly, it is clear that the mutant polymerases in the instant claims and the claims of the ‘649 application are coextensive in scope. The claims differ in that the claims of the ‘649 application do not provide for a fluorescein family dye labeled nucleotide, however Giordano teaches that synthesizing labeled cDNA from an RNA molecule allows use of the cDNA to screen a library of genes thought to contain the gene encoding an RNA of interest (see col 10, lines 3-8). Additionally, Giordano teaches the use of labels such as fluorescein dyes (col. 7, lines 15-20). Therefore, it would have been *prima facie* obvious to one of one of

ordinary skill in the art at the time the invention was made to modify the DNA synthesis reaction of '649 to label cDNA molecules as taught by Giordano. The ordinary artisan would have been motivated to produce labeled cDNA in the methods of '649 for the purpose of providing cDNA which could be used to screen a library of genes for an RNA of interest as taught by Giordano.

The response does not provide any arguments regarding the instant Obviousness type Double Patenting Rejection. The rejection is maintained and made final. With regard to claim 66, it is noted that should applicants overcome the New Matter Rejection set forth above by providing support in the specification, the instant rejection would be applied to claim 66 as well. Finality of the instant office action will not be affected.

### ***Conclusion***

11. No claims are allowed.
12. It is noted that the filing of a declaration under 37 CFR 1.131 cannot be used to swear behind claims directed to subject matter which is claimed by the '193 patent. See MPEP 715 II:

An affidavit or declaration under 37 CFR 1.131 is not appropriate in the following situations:...

(B) Where the reference U.S. patent or U.S. patent application publication claims the same patentable invention. See MPEP § 715.05 for a discussion of "same patentable invention" and MPEP \*> Chapter 2300<.

With regard to claims directed to subject matter claimed in a Publication for Patent, see MPEP 715.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).  
Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1634

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Jehanne Sitton/  
Primary Examiner  
Art Unit 1634  
October 19, 2007